The Termination of the Nerves in the Kidney.

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The animal body, according to more recent investigations is composed of living matter, accumulated in the shape of nodular thickenings, the formerly so called cells, and distributed in a reticular arrangement without interruption throughout all the tissues. It is only the liquid and solid interstitial substances filling the meshes of the living reticulum which are destitute of life and upon the nature of which depends the character of the tissues. Although all living matter is endowed with the property of contractility and irritability, yet all the tissues of the body are connected by means of delicate threads, the nerves, with the central nervous system, the brain and spinal cord. The object of this connection is obviously the regulation of the functions of all the living tissues. The impressions received from the outer world, the disturbances of a pathological nature, such as pain, are carried centripetally, while the impulse of the motor action transferred upon the motor parts, the muscles, run centrifugally. The same is obviously the case in the regulative activity of the process of secretion.

While we know to-day that, with the exception of the horny tissues proper, hairs, nails, etc., all tissues of the body are endowed with life, we are prepared to understand that they are also connected by means of an extremely delicate net-work of nerves with nerve-centres. We are, I think, also justified in assuming that even the small elements or groups of such elements are in connection with the central nervous system. We know, through the researches of Wm. Hassloch, (a) that pretty nearly every cornea-corpuscle is con-

(a). Archives of Opthalmology and Otology; vol. vii, 1878.

nected with a nerve fiber. This helps to explain the very great sensitiveness of this membrane of the eyeball. With the exception of cartilage and bone tissue, known to be rather inert, nerves have been traced into all other varieties of tissue. Muscles, we know, are abundantly supplied with both motor and sensitive nerves. The sensitive nature of the latter is mainly defined by conclusion.

Epithelia are known to be supplied with nerve fibers, particularly the anterior epithelia of the cornea. Since the introduction of the valuable reagent for nerves, the ½ per cent. solution of chloride of gold by Cohnheim (b), the nerve fibers have been traced in different epithelial formations such as the rete mucosum of the skin, the mucosa of the bladder, vagina, etc. Where the ultimate termination of the finest axis fibrillæ ought to be sought for has been a matter for difference of opinion. Some observers have maintained that the ultimate fibrillæ enter the epithelia, and even the neuclei, while others have demonstrated a plexiform arrangement of the nerve fibrillæ between the epithelia.

We know that the activity of the secretory, or glandular, organs is largely under the control of the nervous system. We also know that the activity of a gland depends upon the activity of its single epithelial elements. If, therefore, we observe a decided influence of nervous activity upon the secretory glands, we are inclined to seek for the ultimate terminations of the nerve fibrillæ either in the epithelia themselves, or between them. In the liver I have proved the existence of an extremely delicate reticulated plexus of nerves between the epithelia without having been able to trace them into the interior of these formations (c); and, indeed, the latter feature seems to be entirely superfluous for an understanding of the process of transmitting nervous impulse upon the living matter of epithelia, since we know that the nerve fibrillæ course in the cement substance between the epithelia, and are in direct union with the delicate thread-like formations of living matter which traverse the cement substance and inter-connect all epithelia.

The next subject of my researches was the termination of the nerves in the kidney. R. Heidenhain has recently demonstrated

(b). J. Cohnheim, Virchow's Archives, 1864.

(c). Proceedings of the American Society of Microscopists 1or 1882. Article, Termination of Nerves of the Liver.

that the secretory action of the kidneys is located mainly, if not exclusively, in the epithelia of the convoluted and straight narrow tubules. His experiments with sulphate of indigo and soda proved that the secretion of this coloring matter takes place only in the epithelia of these tubules, while the tuft as such, fully in accordance with the assertions of Bowman, serves merely for the expulsion of water. The epithelia of the uriniferous tubules, as well as the capilliary blood vessel of the tuft, necessarily are under the control of the nerves. My wish and intention were to demonstrate their ultimate distribution in both of these formations. The method resorted to was by staining the sections with the one-half per cent. solution of the chloride of gold, as first suggested by J. Cohnheim. This method has been greatly improved by M. Lowitt (d). Before entering into a discussion of my method I deem it worthy of mention that the nerves in our present understanding of them are formations of living matter, the same as all varieties of tissues. The chloride of gold has the property of staining nerves dark violet more intensely than it has other kinds of living matter, including even muscles, and formic acid removes the gold stain from the latter more readily than from the nerves. This fact would seem to indicate that the nerves are products of living matter in a more concentrated condition than the other tissues, including even muscles. Besides, the interstitial substances in connective tissue, muscle and epithelia, may prevent the gold solution from displaying its full power of reaction, while in the nerve-fiber proper such interstitial substances are wanting or present in only small quantities. Epithelia more particularly we know, are not easily brought under the action of chloride of gold. If treated with formic acid they are attacked sooner than the nerves present between them. Hence the great value of this compound treatment, especially for the bringing out of the nerves. The objects upon which I have made my researches,were the kidneys of the pig, sheep, ox, cat and the human kidney. Among these, those of the pig and the child proved most satisfactory. Of the latter I had at my disposal two kidneys from children, one having died of scarlatina, and the other with diphtheria, and both being involved by a

(d). "Die Nerven der glatten Musculatur." Sitzungsber. d Wiener Akad. d Wissench. lxxi Bd.

morbid process known as acute catarrhal nephritis. The edematous swelling of the connective tissue frame of these kidneys seems to have in a marked degree facilitated the tracing of the nerve fibers, although both were preserved in a half per cent. solution of chromic acid before being subjected to the influence of the chloride of gold.

The fresh kidneys, as well as those preserved in chromic acid solutions were frozen in the freezing microtome of Dr. Taylor, and the sections, cut very thin, were allowed to remain in the gold solution for varying periods of time. Some sections remained in the gold only forty minutes, others several hours; some two days, and a few, one of which proved very good, several days. While in the gold solution they were, of course, kept in a dark place. When removed they were carefully washed in distilled water and placed in strong formic acid of a specific gravity of 120 degrees from five to eight minutes, or in a twenty-five per cent. solution of the same for hours and even days.

Sometimes I obtained very good specimens by placing the sections first in a dilute twenty-five per cent. solution of formic acid, for twenty-four hours, and afterwards staining them with chloride of gold until they reached the color desired. Sections which had been preserved in the chromic acid, required a much longer exposure to the gold than fresh specimens and never took so deep a stain, though the ultimate results were about the same.

I must lay special stress on one fact; that sections from some kidneys invariably assume a dark red or crimson color after being treated with formic acid and these, without exception, proved useless for showing nerves. Those which took on a dark purple tint were the best. In some cases where the sections, after a first treatment with the gold and afterwards with the formic acid, had proved worthless for nerves a second staining with gold was tried without the use of formic acid but only with a washing in distilled water, with very good results. All of the sections were mounted in glycerine and remained unchanged during the period of investigation, which continued for several months.

The nerves supplying the kidneys are mainly of the non-medullated variety. They accompany the larger arteries of this organ,

either in bundles or in flat expanded layers and the latter features I found more common than the former.

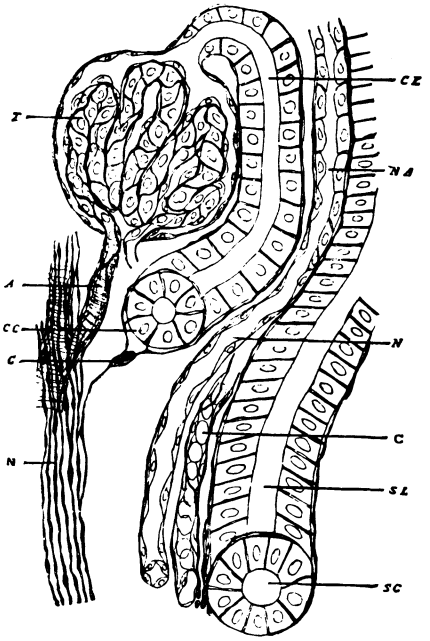

Diagram of the termination of the nerves of the kidney

N. Bundle of non-medullated nerve-fibers accompanying an artery.
T. Tuft.
A. Afferent vessel.
G. Ganglionic enlargement along a nerve-fiber going to a convoluted tubule.
C. L. Convoluted tubule in longitudinal section.
C. C. Convoluted tubule in cross section.
N. A. Ascending branch of narrow tubule.
N. Narrow looped tubule.
C. Capillary blood vessel.
S. L. Straight collecting tubule in longitudinal section.
S. C. Same in crop-section.

Sometimes an artery would be found encircled by a net-work of non-medullated nerves of a bewildering number. Hundreds of such nucleated bundles of fibers could be traced around, above and below an artery, freely branching, bifurcating and supplying all the neighboring formations with a large number of delicate fibrillæ. In such a case the single non-medullated nerve-fibers lay apart and were separated by an extremely delicate layer of fibrous tissue, the

perineurium internum. The corticle substance undoubtedly derives all of its nerves from such bundles accompanying arteries. The pyramidal substance is supplied with bundles of non-medullated nerves, apparently independent of the arteries; at all events such formations are exceedingly scanty here. The bundles of non-medullated nerve-fibers are marked by a large number of nuclei.

True ganglions I have seen only in small numbers.

The bundles of nerve-fibers give off delicate ramules to the afferent vessels by which they enter the tuft, and here they produce a delicate plexus spun around the capillaries of the tuft. It was impossible to decide where the ultimate fibrillæ branch in the capillaries, of the tuft, because in the specimens treated with formic acid it was impossible to distinguish between the flat epithelia covering the convolutions of the capillaries and the endothelia covering their interior. Sometimes I obtained a specimen in which it seemed as if the ultimate fibrillæ branched beneath the covering, flat epithelia in the delicate connective tissue between the convolutions of the capillaries, but of this I am not certain. I wish here to corroborate the assertions of L. Bremer (e) that every capillary is supplied with a plexus of non-medullated nerve fibrillæ, but I disagree with his assertions, that the nerves run outside the wall of the vessel, and do not penetrate the wall itself. My own observations, I think, leave little doubt that they penetrate the cement substance between the endothelia. Concerning the distribution of the nerves in the middle coat of the arteries, I fully agree with the assertions of M. Lowitt (f) that they run between the smooth muscle fibers. From the large bundles of non-medullated nerve fibers, innumerable, delicate, beaded fibrillæ arise and course in the delicate, fibrous connective tissue between the uriniferous tubules.

In perfect specimens there is no difficulty in satisfying one's self of the fact, that every tubule is encircled by a plexus of non-medullated nerve fibers coursing either in the immediate vicinity of the tubule, in the interstitial connective tissue, or within the dense layer, subjacent to the epithelia, known as *membrana propria*,

(e) L. Bremer, Archives of Microscopic Anatomy, Bd. xxi, Die Nerven der Capillaren der kleineren Arterien und Venen, 1882.

(f) Die Nerven der glatten Musculatur Sitzungsber. d Wiener Akad. Wissensch. lxxi Bd.

or even within the layer, along the feet of the epithelia themselves. Obviously those nerves are most favorable for research which course outside of the epithelia at a small distance from the membrana propria. Here we can, sometimes, see at certain regular intervals, arising at right or acute angles, extremely delicate nerve fibrillæ which pierce the membrana propria and run into the cement substance between the epithelia. The distance in which these ultimate fibrillæ arise, fully correspond to the breadth of a single epithelial element; so much so that in some places the impression of a ladder with regular rounds is obtained. Of course, only one of the frames or side pieces of the ladder is present.

In a front view of the epithelia the nerve fibrillæ can sometimes be traced in the form of a delicate plexus distributed in the epithelia, and not infrequently conveying the impression that every epithelium is surrounded by a nerve fibrillæ in the cement substance.

In an edge view, this impression is not obtained, for we can see the interstices between the epithelia supplied with nerves only exceptionally, while in the majority of cases two or three epithelia seem to be supplied with only one nerve fibrillæ common to them. The latter image is more particularly pronounced along the straight collecting tubules in which, usually in edge view, two nerve-fibrillæ are situated between three or four epithelial elements; and here the cement substance, carrying the nerve-fibrillæ, is much broader than the cement substance apparently destitute of nerve fibers. If, however, we recall the fact, that in a front view of the tubules, the arrangement of the ultimate fibrillæ is plexiform, we obviously should not expect to see in edge view, nerve-fibrillæ between each single epithelium.

The distributions of the nerves in the uriniferous tubules seems to be richer in the convoluted and the ascending and decending limbs of the narrow tubules, while the straight collecting ones seem to be more scantily supplied. Several times I have seen nerve-fibers accompanying the loops of the narrow tubules in a direction corresponding to their course.

Recent researches made by S. Stricker (g) make it evident that the cement substance between the epithelia is by no means an

(g) Mittheilung uber Zellen und grund Substanten. Wiener Mediz. Jahrbucher, 1880.

invariable formation, and that temporarily the ledges of the cement substance may be distinctly seen; at other times, on the contrary, it is lacking to such an extent that the epithelia represent one unbroken layer of protoplasm with nuclei at regular intervals. Even when the cement substance is apparent, invariably transverse spokes (the formerly so called thorns) are seen traversing the layers of cement substance interconnecting the single epithelia. It is these spokes with which the nerve-fibrillæ inosculate. Thus we easily understand the way in which nervous impulse is transmitted into the interior of the small secretory work shops, termed epithelia.

Dr. Beale (h) claims to have traced the nerves of the kidney to their distribution around the vessels and uriniferous tubules, but makes no mention of their final endings. The low power objectives used by him leads me to think he may have mistaken connective tissue-fiber for nerves.

(h) Kidney Diseases, Urinary Deposits and Calculous Disorders by Lionel S. Beale, M. B., F. R. S. 3d Edition, 1869.